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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
08/959,013	10/28/97	O'MALLEY	B	226/286

EXAMINER	
HAYES,R	
ART UNIT	**PAPER NUMBER**
1647	14

022249
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HM22/1025

DATE MAILED: 10/25/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/959,013	O'Malley et al
Examiner	**Group Art Unit**
Robert C. Hayes	1647

☒ Responsive to communication(s) filed on *Jul 6, 2000* .

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *11-14, 30, 31, and 41-45* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *11-14, 30, 31, and 41-45* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *13*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

1. The amendment filed 7/06/00 has been entered.

2. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1647.

3. The rejection of claims 13-14 & 31 under 35 U.S.C. 101 for non-statutory subject matter is withdrawn due to the amendment of the claim.

4. The rejection of claims 11-12 under 35 U.S.C. § 112, second paragraph, as being indefinite for being dependent on nonelected base claims, is withdrawn due to the amendment of the claims.

5. Applicant's arguments filed 7/06/00 have been fully considered but they are not deemed to be persuasive.

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. The Declaration under 37 CFR 1.132 filed 7/6/00 is insufficient to overcome the rejection of all pending claims as set forth in the last Office action because the current application is directed toward isolated nucleic acid molecules and not "methodology described in the 08/454418 application", which further is not claimed as a priority application. Thus, because Declarant's arguments are not related to the subject matter claimed in the instant application, they are not persuasive.

8. Claims 30-31 stand provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 61-62 of copending Application No. 08/479913, for the reasons made of record.

9. Claims 11-14 and 41-45 are provisionally rejected under the judicially created doctrine of double patenting over claims 32, 37-49, 51-54, 56-57 & 64-66 of copending Application No. 08/479913, for the reasons made of record for claims 11-14.

10. Claims 11-14, 30-31 and 41-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid encoding the modified glucocorticoid receptor protein contained within plasmid pGR0403R (i.e., from SEQ ID NO 1), does not reasonably provide enablement for claims to any biologically functionally equivalent plasmid or DNA molecule with no recited structural characteristics. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the reasons made of record for claims 11-14 & 30-31, and as follows.

Applicants argue on pages 6-7 of the response that "Applicant notes that this argument appears to be inconsistent with the Examiner's obviousness argument", and cites *In re Angstadt and Griffin*, and *In re Fuetterer*. In contrast to Applicants' assertions, the pending claims are not directed toward "combination[s]" of "inorganic salts", which have known structures (i.e., as it relates to *In re Fuetterer*). Moreover, obviousness is not a criteria for assessing enablement under 35 USC 112, first paragraph. As Applicants are fully aware, the undue breadth of the claims encompass obvious nucleic acid species known in the art, which is the subject matter for the rejection set forth below. Thus, no inconsistency exists. The issue pending here is that without sufficient structural characteristics by which one can visualize the nucleic acids currently claimed, one skilled in the art would know how to make and use the currently claimed generic nucleic acids without requiring undue experimentation to first discover what structurally constitutes the claimed nucleic acid sequences; thereby, not meeting the requirements of 35 USC 112, first paragraph. Accordingly, it was held in *Ex parte Maizel* (27 USPQ2d 1662 at 1665) that:

> Appellants have not chosen to claim the DNA [product] by what it is but, rather, by what it does, i.e., encoding either a protein exhibiting certain characteristics, *or* a biologically functional equivalent thereof. Appellants' claims might be analogized to a single means claim of the type disparaged by the Court of Customs and Patent Appeals in *In re Hyatt,* 708F.2d 712, 218 USPQ 195 (Fed. Cir. 1983).

> The problem with the phrase "biologically functional equivalent thereof" is that it covers any conceivable means, i.e., cell or DNA, which achieves the stated biological result while the specification discloses, at most, only a specific DNA [product] segment known to the inventor. Clearly the disclosure is not commensurate in scope with the claims."

In summary, the specification describes a single nucleic acid molecule encoding a single glucocorticoid receptor protein (e.g., plasmid pGR0403R of SEQ ID NO 1). However, the name "a plasmid designated as pGR0403R", or a nucleic acid encoding a "modified glucocorticoid receptor protein", sets forth no structural characterization and little functional characteristics, and encompasses any random mutation to the single disclosed nucleic acid of SEQ ID NO:1, which would be expected to encode inactive proteins; consistent with the teachings of Rudinger previously made of record. Moreover, the specification does not teach which particular nucleotides are required for encoding a glucocorticoid receptor protein with any activity. Nor does the specification disclose those encoded amino acid residues critical for ligand/agonist/ antagonist binding, or those "modified" encoded amino acid residues that can give rise to a functional glucocorticoid receptor protein, which distinguishes the instant invention from any different nucleic acid encoding a modified steroid hormone receptor protein. Thus, Applicants' argument are not persuasive.

11. Claims 11-14 and 41-45 are rejected under 35 U.S.C. § 102(b) as being anticipated by Evans et al. US Patent 4,981,784), or by Hollenberg et al. (1987), or by Lanz et al. (1994), for the reasons made of record for claims 11-14, and as follows.

Applicants argue on pages 8-9 of the response that "Evans is in no way directed toward, and utterly fails to disclose the modified steroid hormone receptors of the instant invention...". However, in contrast to Applicants' assertions, in that the claims merely recite "capable of...", and because no claim limitations that exclude ligand binding domains selected from the group of "wildtype receptors" are recited in the current claims, Applicants' arguments are not persuasive. Note that Evans LBDs are not "naturally occurring", by definition, because Evan's chimeric constructs are not "naturally occurring", by definition.

Applicants then argue that "Hollenberg utterly fails to disclose the modified steroid hormone receptors of the instant invention". In contrast to Applicants' assertions, Hollenberg's LBDs are not "naturally occurring", by definition, because Hollenberg's chimeric constructs are not "naturally occurring", by definition, and contain the recited mutated "ligand-binding domain (the C-terminal), as currently recited in the claims. Therefore, because all recited structural limitations are met by Hollenberg's constructs, the recitation of merely requiring "capable of... binding non-natural ligands", is reasonable; absent evidence to the contrary.

Applicants finally argue that "[t]he Lanz et al. paper also fails to anticipate the claimed invention". In contrast to Applicants' assertions, Lenz's chimeric constructs are not "naturally occurring", by definition, and contain the recited generic "mutations". Therefore, because all recited structural limitations are met by Lanz's constructs, and because no negative teachings are contained within Lanz's paper that "appear to teach away from the [structurally undefined] invention", the recitation of merely requiring "capable of... binding non-natural ligands" is

reasonable; absent evidence to the contrary. It is further noted that no where in the claims is there any recitation for "mutations in the glucocorticoid ligand binding domain that *do not allow* binding of a non-natural ligand"[emphasis added].

Accordingly, the courts have held that

"the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Accordingly, since the issue in the present appeal is whether the prior art factor is identified or patently indistinct from that of the material on appeal, appellants have the burden of showing that inherency is not involved". *Ex parte Gray,* 10 USPQ 2d 1922 (1989); *In re Best,* 195 USPQ 430 (CCPA 1976).

Further, the courts have held that "when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product..., a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable". *In re Brown*, 173 USPQ 685 (1972).

In summary, Evans et al. teach plasmids that contain modified steroid hormone receptor proteins (see columns 4, 7-8, 10-12, 17-20). In particular, modified plasmids were constructed that swap functional domains for estrogen, glucocorticoid, mineralocorticoid, thyroid hormone and retinoic acid receptors (i.e., encoded "modified" glucocorticoid receptors (e.g., column 17, lines 16-39). In that CV-1 cells (i.e., a transformed mammalian cell line) were transfected with the expression plasmids encoding these chimeric receptors(i.e., as it relates to claims 12-14 & 45), all structural limitations of the claims are met.

Hollenberg et al. teach a number of modified glucocorticoid receptor comprising deletion mutants, which appear to encompass all claim limitations of nonelected claims 6-9 (pg. 41, Figs 1-2). In that these representative DNA sequences were transfected/transformed into CV-1 host cells (e.g., Fig. 2 and pg. 45), the limitations of claims 12-14 & 45 are also met.

Lanz et al. teach glucocorticoid expression constructs (i.e., vectors containing modified glucocorticoid receptor nucleic acid molecules) that encode modified glucocorticoid receptors that are responsive to the antagonist, RU486, but no longer react to the agonist, dexamethasone (e.g., pg. 2183-2185 & 2187-2188; fig. 1 and Table 1). In that these constructs are transfected into CV-1 host cells, all structural limitations of the claims are met.

12. Claims 30-31 stand rejected under 35 U.S.C. § 103 as being unpatentable over Hollenberg et al., or over Lanz et al.

Applicants' argue on page 10 of the response that "[c]laim 30 is directed toward a plasmid designated as pGR0403R", and cites *In re Deuel*. However, because no structural characteristics (e.g., of SEQ ID NO:1) are recited in the claims to distinguish the pGR0403R plasmid currently claimed from those of Hollenberg et al., or over Lanz et al., Applicants' arguments are not persuasive, for the reasons made of record.

Accordingly, the courts have held that

"the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Accordingly, since the issue in the present appeal is whether the prior art factor is identified or patently indistinct from that of the

material on appeal, appellants have the burden of showing that inherency is not involved". *Ex parte Gray,* 10 USPQ 2d 1922 (1989); *In re Best,* 195 USPQ 430 (CCPA 1976).

Further, the courts have held that "when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product..., a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable". *In re Brown*, 173 USPQ 685 (1972).

In summary, Hollenberg et al. and Lanz et al. are as set forth above. However, neither Hollenberg nor Lanz specifically call their plasmid constructs, pGR0403, even though they do appear to disclose an equivalent constructs, e.g., pRShGRα (Fig. 2 and pg. 45 of Hollenberg), and, e.g., CS1/CD (pg. 2187 and Fig. 1c of Lanz).

It would have been obvious to one or ordinary skilled in the art at the time of filing Applicants' invention to use any vector well known in the art that can transfect the CV-1 host cells of Hollenberg or Lanz, for cloning the modified glucocorticoid receptor DNA of Hollenberg or Lanz, including the same vector as used in the construction of plasmid pGR0403R, because use of vectors to express equivalent DNA sequences encoding modified glucocorticoid receptors with equivalent function activity are well known in the art, and merely increase the variety of cells that this construct can successfully transform (i.e., CV-1 host cells). It is further noted that the vector used for construction of plasmid pGR0403R was not disclosed in the instant application, and therefore, appears equivalent to the plasmid construct of Hollenberg or Lanz, and therefore, obvious; absent evidence to the contrary.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternative Fridays, from 8:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
October 23, 2000

GARY L. KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600